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10/601,072	06/19/2003	Jean-Philippe Girard	ENDOC.009CP1	5184

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EXAMINER	
YAO, LEI	
ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/601,072	GIRARD ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15, 17-20, 22, 24-28, 92, 94-105, 107-113, 115-121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17-20,22,25,26,28,92,94,96,98-105,107,109,110,112,113,115,117 and 119-121* is/are rejected.

7)☒ Claim(s) *24,27,95,97,108,111,116 and 118* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

Response to Amendments and Arguments

The Amendment filed on 8/1/2008 in response to the previous Non-Final Office Action (2/7/2008) is acknowledged and has been entered.

Claims 1-14, 16, 21, 23, 29-91, 93, 106, 114 have been cancelled.

Claims 15, 17-20, 22, 24-28, 92, 94-105, 107-113, 115-121 are pending and examined on the merits for the method of binding or inhibiting the activity of chemokine comprising contacting the chemokine with the polypeptide of SEQ ID NO: 3 or its variants.

Rejection Maintained and Response to Arguments

Rejection under **first paragraph of 35 U.S.C. 112**:

> **The following is a quotation of** the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection- *A method drawn to a method encompassing a polypeptide having at least 95% identity to SEQ ID NO: 3 or to the chemokine binding domain (143-213 of SEQ ID NO: 3).*

Claims 15, 17-20, 22, 25, 26, 28, 92, 94, 96, 98-105, 107, 109, 110, 112, 113, 115, 117, 119-121 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention reformed based on the amendment as thte following:

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The specification must describe the claimed invention in sufficient detail for the claimed invention comprising the process and genus of the products used in the process. Possession may be shown, for example, by describing an actual reduction to practice of the claimed invention. A specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose.

In this case the claims are broadly drawn to a method of binding or inhibiting a activity of a chemokine comprising contacting to a chemokine of comprising SLC/CCL21 CCL19, CCL5, CXCL9 and CXCL10 etc with a THAP1 polypeptide comprising the full length of SEQ ID NO: 3, chemokine binding domain (143-213 of SEQ ID NO: 3) or their homologies (95% or more sequence identity). Thus, the claims are inclusive of variant polypeptides that are 95% identical to the amino acids of SEQ ID NO: 3 or the domain of 143-213 of SEQ ID NO: 3 in the method for binding or inhibiting an activity of a chemokine by contacting to any of the known chemokines.

The figure 12 of the specification describes the polypeptide fragments of THAP1 (SEQ ID NO: 3) and the chemokine-binding domain of THAP1 (143-213 of SEQ ID NO: 3) associated with the chemokine SLC-binding. The figure 19, teaches that the THAP1-GST fusion protein binds to a few more chemokines comprising CCL5 and SLC. The examples 33-37 teach the chemokine activity is inhibted by THAP1 of SEQ ID NO: 3. The specification does not provide a teaching that the other faimily members of THAP

proteins having 95% identity to the THAP1 of SEQ ID NO: 3 could perform the same binding and inhibitory activity to the same chemokines listed in the claims.

Regarding the binding of a chemokine to the variants of THAP1 having 95% identity to the THAP1 of SEQ ID NO: 3 or the chemokine binding domain, figure 9 -10 although provide sequence alignment of THAP protiens, which have the homologues at the C-terminus, the application does not reduce to practice or describe which amino acids or domain are responsible for these chemokine binding. The figure 12 of the specification teaches C-terminal fragments of THAP1, as a chemokine binding domain (143-213 amino acids of SEQ ID NO: 3) being responsible for the SLC/CCL21 binding, the full length THAP1 (213 amino acids) with a deletion of five amino acids at position 168-172, ΔQRCRR in the binding domain, which counts more than 95% sequence identity to SEQ ID NO: 3, shows no binding activity. Thus, the specification itself has suggested that not all the polypeptide having more than 95% identity to the sequence of SEQ ID NO: 3 has the binding ability to the chemokine, SLC/CCL21.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics. i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or

disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The specification provides neither a representative number of polypeptides that encompass the genus that reveal the roles of these polypeptides in the binding and inhibition of the activity of any chemokine, nor does it provide a description of structural features that are common to the polypeptide having at least 95% homology to amino acid sequence 143-213 of SEQ ID NO: 3 that could inhibit any activity of the chemokines. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of the species of polypeptide is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the applicants, at time of filing the application, do not have the possession of claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) and functional attribute(s) of the encompassed genus of polypeptides or the chemokines, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the THAP1 protein of SEQ ID NO: 3, and the chemokine binding domain of 143-213 of SEQ ID NO: 3 that bind to the chemokines listed in the claim 15, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In the remarks filed with this amendment, applicant request to withdraw the rejection by indicating the support from the specification. This has been carefully reviewed and the support has been discussed in the rejection above.

Scope of Enablement Rejection *-A method drawn to inhibiting any chemokine activity by the peptide having 95% identity to SEQ ID NO: 3 or the chemokine binding domain (143-213 of SEQ ID NO: 3).*

The rejection is reformed based on the amendment.

Claims 15, 17-20, 22, 25, 26, 28, 92, 94, 96, 98-105, 107, 109, 110, 112, 113, 115, 117, 119-121 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of binding and inhibiting the chemokine activities by contacting the THAP1 protein of SEQ ID NO: 3 (full length) or its chemokine binding domain (143-213 of SEQ ID NO: 3), does not reasonably provide enablement for the method of binding or inhibiting the activities of the chemokines with any other

peptide having 95% or more sequence identity to the THAP1 of SEQ ID NO: 3 or its chemokine binding domain (143-213 of SEQ ID NO: 3).

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands*, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are broadly drawn to a method of inhibiting the activity of the chemokines listed in the claim 15 and 101 comprising contacting or binding the chemokines with an agent comprising polypeptides having at least 95% amino acid identity to the sequence of SEQ ID NO: 3 or its chemokine-binding domain (143-213 of SEQ ID NO: 3), wherein the activity of said chemokine is inhibited. However, the specification, on page 230 (example 15-17), teaches only THAP1 protein of SEQ ID NO: 3 and its chemokine binding domain (143-213 of SEQ ID NO: 3) binding to the chemokines. The specification does not provided teachings on the inhibiting the activity of the chemokines by contacting and binding to the THAP1 homologies having 95% sequence identity to SEQ ID NO: 3 or to the chemokine binding domain (143-213 of SEQ ID NO:3) and does not provide objective evidence showing all the THAP peptides listed in the specificiaton or any peptide having 95% of sequence identity to the SEQ ID NO: 3 or its binding domain have the same bidning and inhbitory activity as the THAP1 of SEQ ID NO: 3. In addition the instant specification in figure 12 teaches that the full length THAP1 (213 amino acids) with a deletion of five amino acids at position 168-172, ΔQRCRR, which counts for less than 5% the amino acid difference compared to SEQ

ID NO: 3, does not have the binding ability to SLC chemokine. Thus, the specification self has suggested that not all the peptides that are more than 95% identity to SEQ ID NO: 3 have the binding capacity to the chemokines and the specification fails to provide enablement disclosure for claimed invention which one skilled in the art could use the invention without undue a quantity of experimentations.

It is also know in the art that even a single modification or substitution in a protein sequence can alter the protein function. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al, Journal of Cell biology, Vol 111, p2129-2138, 1990, provided in the Office Action 07/27/2006). Removal of the amino terminal histidine of glucagons substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin et al Biochemistry USA, vol 14, p1559-1563, 1975, provided in the Office Action 07/27/2006). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein.

In view of the lack of guidance, lack of examples, and lack of predictability and objective evidence showing that the variant of THAP1 of SEQ ID NO: 3 or the chemokine binding domain having 95% sequence identity could bind to the chemokines and inhibit their activities, one skilled in the art would not know how to use the claimed invention based on the teachings in the prior art or instant specification and under a quantity of experimentations would be forced.

In the remarks filed with this amendment, applicant requests to withdraw the rejection in view of providing the supports for the claimed invention from the specification. This has been carefully reviewed and discussed in the rejection above. The remarks mention the declaration of Dr Jean-Philippe Girard filed on 10/30/2007,

that has been reviewed and refers to the assay of chemokine bindings of the THAP1 (SEQ ID NO: 3) protein, which could not overcome the rejection for the binding and inhibition of the chemokine activity by 95% sequence identity to the peptide of SEQ ID NO: 3 or to its binding domain as set forth above.

Claim Objections

Claims 24, 27, 95, 97, 108, 111, 116, 118 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claim is allowed.

Claims 15, 17-20, 22, 25, 26, 28, 92, 94, 96, 98-105, 107, 109, 110, 112, 113, 115, 117, 119-121 are rejected.

Claims 24, 27, 95, 97, 108, 111, 116, and 118 are objected to.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643